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GRANT NUMBER DAMD17-94-J-4279

TITLE: Follow-Up Care for Older Women With Breast Cancer

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REPORT DATE: August 1997

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	August 1997	Annual (1 Aug 96 - 31 July 97)

4. TITLE AND SUBTITLE
Follow-Up Care for Older Women With Breast Cancer

5. FUNDING NUMBERS
DAMD17-94-J-4279

6. AUTHOR(S)
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
New England Medical Center
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, MD 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200*

Little is known about what constitutes appropriate care for older women with breast cancer. Extending work begun as part of an National Cancer Institute-funded project, we are examining whether variations in care received by older women affect short-term psychosocial and clinical outcomes. Our specific aims are: 1) To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies; 2) To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis; and 3) To determine the effects of ongoing breast cancer care on patients' quality of life. We are conducting a longitudinal observational study of a cohort of 302 women ≥ 55 years of age diagnosed with stage I and II breast cancer between October 1992 and December 1995 at five sites in Boston, Massachusetts. Women are interviewed annually to obtain information about health and personal characteristics. Medical record abstracts are performed annually to gather information about treatments received, tests performed, and disease recurrences. Descriptive and multivariate analytic techniques will be used to identify patient and provider characteristics associated with variations in care received and the effects of these variations on patients' quality of life.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Health Services Research, Elderly, Quality of Life, Humans, Observational Study, Breast Cancer	77
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

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Sherrie H. Kaplan

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5. INTRODUCTION

Nature of the Problem

Little is known about what constitutes appropriate care for older women with breast cancer (1) because until recently, women ≥ 70 years of age were excluded from most clinical trials. It is perhaps not surprising, therefore, that there is considerable variation in how older women are treated (2-9). There are several reasons why careful longitudinal observational studies involving older women with breast cancer need to be performed. First, because of spiraling health care costs, Congress and third party payers are demanding that we determine, insofar as possible, what constitutes effective care for our patients. Although randomized clinical trials will continue to be the gold standard for assessing treatment efficacy, large numbers of older women are not likely to be enrolled in such clinical trials and those that are enrolled will not be representative of those cared for by most practicing physicians (1). Second, the variations in diagnostic evaluation and initial treatment that have been observed may or may not matter in terms of important short and long-term clinical outcomes (recurrence and mortality) and in terms of psychosocial outcomes (physical, social, and emotional function). Evidence linking variations in care received by older patients and variations in clinical and psychosocial outcomes is sparse. For example, only very recently has the first study been published which links nondefinitive therapy with an increased risk of mortality (10). In addition there are limited data regarding psychosocial outcomes. However, there is evidence to suggest that more extensive surgery is a risk factor for poor upper body function among older women, but not for poor emotional function (11). Because of the chronic nature of early stage breast cancer, what happens in terms of follow-up care (adjuvant therapy and surveillance testing) may have a greater effect on patients' well-being than initial treatment. Third, because the incidence of breast cancer is continuing to rise, because the incidence increases with age (12), appearing only to level off at about age 80-85 (13), and because the numbers of women 65 years of age are rapidly increasing, the absolute number of new breast cancer cases will continue to grow into the foreseeable future, as will the proportion of cases involving older women.

Background/Previous Studies

The current study is designed to identify determinants of variations in adjuvant hormonal/chemotherapy and follow-up care among older women with early stage breast cancer and the effects of these variations on health-related quality of life and breast cancer-specific function.

Adjuvant Tamoxifen Therapy has both Benefits and Risks/Barriers

Benefits. Adjuvant tamoxifen therapy has been shown to decrease both rates of recurrence and mortality in older women with early stage breast cancer. A meta-analysis of clinical trials worldwide that included 2656 women ≥ 70 years of age, documented decreases in both recurrence (28%) and overall mortality (21%) rates among patients with node-positive disease treated with tamoxifen. Similar proportional risk reductions were found for node-negative

patients, although the absolute risk reduction was greater for women who were node-positive. In addition, the magnitude of risk reduction, both with respect to recurrence and mortality, was similar across three postmenopausal age groups: 50-59, 60-69, and 70+. Adjuvant tamoxifen therapy also was beneficial for women with hormone receptor-poor tumors, albeit to a lesser extent than in those with hormone receptor-rich tumors. Treatment with tamoxifen also prevents the development of contralateral breast cancer (14). There are non-breast cancer benefits of therapy for postmenopausal women as well. Tamoxifen may prevent osteoporosis (15) and lower cholesterol levels (16). Recent reports from Europe suggest that tamoxifen reduces the risk of hospitalization for cardiovascular disease and for fatal myocardial infarction (17-18).

Risks/Barriers to Treatment. Tamoxifen is prescribed as the result of a definite disease (breast cancer) in order to reduce the probability of events in the future: breast cancer recurrence; the development of contralateral breast cancer; death; and possibly, cardiovascular and osteoporotic complications. Although there are proven health benefits, the risks and costs are not insignificant. First, although some Medigap policies include a prescription medication benefit, many do not; most older persons must pay out-of-pocket for their medications, many of which cost a dollar or more per day (e.g., 19, 20). Generic tamoxifen, at the recommended dose of 20 mg/day, will cost most patients $85/month or more over a two to five year period. Second, taking tamoxifen may make patients feel worse, not better. One clinical trial involving younger postmenopausal women documented about a 4% dropout rate due to side effects, including nausea, hot flashes, edema, and vaginitis (21). Another clinical trial, also involving women < 65 years of age, documented persistent vasomotor, gynecological, or other major side effects in 48% of tamoxifen treated women compared with 21% of controls. Moderate to severe hot flashes, for example, persisted for 12 months in 22% of tamoxifen subjects vs. 5% of controls (22). In a clinical trial of women 65 - 84 years of age, Cummings and colleagues noted that 42% of women taking tamoxifen experienced mild toxicity symptoms by Eastern Cooperative Oncology Group criteria (mild, moderate, and severe), 21% experienced moderate symptoms, and 3% experienced severe symptoms (23). Third, treatment with tamoxifen increases the risk of rare, but serious illnesses. Deep vein thrombosis can complicate the use of tamoxifen and this risk appears to be greater in women ≥ 65 years (24). In addition, recent studies from Europe and the United States are relatively consistent in demonstrating an increased risk of endometrial cancer among tamoxifen users (25, 26). About 75% of endometrial cancers occur in women ≥ 60 years of age , and this already elevated base rate appears to be more than doubled by the addition of tamoxifen treatment (26). In light of the growing body of information about the risk of endometrial cancer, annual gynecological examinations, ranging from a history and physical examination to pelvic and/or endovaginal ultrasound and/or endometrial sampling are recommended for patients receiving tamoxifen (26). However, there is uncertainty as to the best approach to surveillance (27-29).

Evidence for Adjuvant Chemotherapy Treatment Efficacy

The value of adjuvant chemotherapy with or without tamoxifen in postmenopausal women is controversial, and in women over 70 years of age, has not been well-studied. In the meta-analysis described above, adjuvant chemotherapy resulted in only a 10% reduction in the mortality of women aged 60-69, although recurrences were reduced significantly. There were

only 274 women enrolled in chemotherapy trials who were ≥ 70 years of age, and in these, adjuvant chemotherapy did not appear beneficial (14). Clearly adjuvant chemotherapy cannot be considered standard treatment for postmenopausal women, especially those ≥ 70 years of age. It is possible, however, that adjuvant chemotherapy may be of benefit to subgroups of patients, especially those with aggressive disease. Because so little is known about the use of chemotherapy in older persons, the current project is addressing the following descriptive questions: 1) What proportion of older women, both with stage I and stage II breast cancer, currently receive adjuvant chemotherapy? and 2) What patient and physician characteristics are associated with the receipt of chemotherapy?

Surveillance for Recurrence following Initial Therapy

Although women are routinely followed by clinical examination and laboratory testing for evidence of recurrence, there is no evidence that this strategy results in earlier detection of recurrence or reduces mortality (30). Furthermore, case series evaluating the yield of various screening strategies have documented that most recurrences are detected either by patients themselves or by clinical examination (31-35). Only about 15% of recurrences are detected by surveillance testing which, in 1990 dollars amounts to an annual cost of about $1200/patient. No published studies have examined the costs and benefits, in human terms (either increasing anxiety or allaying fears), of surveillance testing, although a clinical trial evaluating these issues is reported to be in progress (35). Furthermore, none of the published studies have involved older women. Information about surveillance testing in older women is conspicuously lacking, including the types and frequency of testing and its impact on patient outcomes, particularly psychosocial outcomes. The current study is addressing the following questions: 1) How often are patients being seen and by which physicians during the early years following primary treatment? and 2) What are the types and frequency of surveillance tests and what are the effects of this testing on patient outcomes?

Summary: Given the national mandate to determine what constitutes effective health care and the fact that breast cancer is a disease primarily of older women (nearly half of newly diagnosed cases of breast cancer occur in women ≥ 65 years of age), we are conducting a longitudinal study of newly diagnosed older women with stage I and II disease: 1) to identify variations in follow-up care, and 2) to link these variations to patient outcomes. In conjunction with limited clinical trial data, this will be valuable information to assist clinicians in medical decision-making. Together, these two types of data will be able to inform the development of guidelines for the care of older women with breast cancer.

Purpose of the Current Study

As described above, we are filling important gaps in knowledge by addressing the following **study questions** in our current study:

1. What patient and provider characteristics are associated with the receipt of hormonal and/or chemotherapy?

2. What are the effects of hormonal treatment on patients' quality of life?
3. What patient and provider characteristics are associated with the receipt of surveillance tests?
4. What are the effects of surveillance testing on patients' quality of life?

Our specific aims are:

1. To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies.
2. To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis.
3. To determine the effects of ongoing breast cancer care (adjuvant therapy and disease surveillance) on patients' quality of life.

Overview of Methods of Approach

As described in more detail below (**6. BODY**), we are studying a cohort of women ≥ 55 years of age with newly diagnosed early stage breast cancer over a 2-5 year time period. Initial telephone interviews are conducted at 3-5 months following initial definitive treatment, with subsequent interviews occurring approximately two years later, and annually thereafter. Medical records are abstracted, beginning at the time of diagnosis and continuing until project completion, or the development of metastatic disease or subject death. The medical record review covering the initial treatment period and the baseline interview were funded by the National Cancer Institute. The follow-up interviews and medical record reviews are funded under the current project by the US Army Medical Research, Development, Acquisition and Logistics Command.

6. BODY

Overview and Summary of Parent Study Funded by the National Cancer Institute (CA57754)

Funding from the National Cancer Institute (NCI) enabled us to enroll the cohort that is being followed longitudinally for the current project. Patients ≥ 55 years of age with newly diagnosed early stage breast cancer, being cared for at one of five hospitals with academic affiliation in Boston, Massachusetts, were enrolled between January 1993 and April 1996. Eligible patients were sent an introductory letter signed by their surgeon and a consent form approximately three months following initial surgical treatment. This was followed by a telephone call from our interviewer who further explained the study, answered questions, and obtained informed consent. Data were collected via a review of patients' surgical records, and a 30 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: histology, stage, estrogen receptor status, surgery performed, additional therapies received, and medical comorbidities.

Our patient telephone interview included questions about: general health-related quality of life, breast cancer-specific quality of life, medical comorbidities, the treatment decision-making process, treatment priorities, perceptions of doctor-patient communication, and demographic characteristics.

Results. Our overall response rate was 78%. Of 387 eligible patients, 302 participated. The number of participants was less than originally projected due to a smaller number of eligible patients from which to draw. This circumstance was due in part to the departure from Boston of three well-known and established breast cancer surgeons. Non-participants were older (mean age=71.2 years for non-participants; =68.4 years for participants), but there was no difference in the proportion of participants and non-participants with stage I and stage II disease.

Descriptive data on the 302 patients enrolled are presented in Table 1. A little over half of our subjects are ≥ 65 years of age and most are white. Half are married; most of the remainder are widowed. The majority have a high school education or greater. Our measure of comorbidity is a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related symptoms. In this sample the average score was 7.06 and ranged from 3.0 to 20. Positive scores reflect above average comorbidity. In addition, the majority of patients have infiltrating ductal carcinoma and have stage I disease. Of interest, stage I patients tend to be slightly older than stage II patients (68.9 vs. 66.6 years for mean age), perhaps reflecting the increasing use of mammography in older women.

In contrast to patterns of care observed elsewhere among older women with breast cancer, the majority of our patients underwent breast conserving surgery and axillary dissection, followed by radiation therapy (Table 2). Only a quarter received a modified radical mastectomy. The remaining quarter received: 1) breast conserving surgery and radiation therapy, but no axillary dissection (n=26), 2) breast conserving surgery and axillary dissection, but no radiation therapy (n=22), 3) breast conserving surgery alone (n=10), or 4) other (n=10), including radiation therapy only, incisional biopsy only, and simple mastectomy with or without radiation therapy.

Factors Associated with the Receipt of Standard Primary Tumor Therapy.

To identify factors associated with the receipt of standard primary tumor therapy (modified radical mastectomy or breast conserving surgery and axillary dissection followed by radiation therapy), we examined the relationship between four categories of independent variables and this outcome. These four categories included: 1) demographic characteristics: age (55-64, 65-74, 75+), marital status (married/not married), and education (< high school/ ≥ high school); 2) health status: comorbidity (a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related symptoms that were part of the Total Illness Burden Index (36), with a positive score reflecting above average comorbidity) and physical function (a continuous variable, a subscale of the SF-36 (37) which is scaled from 0-100 with a higher score indicating better function); 3) tumor characteristics: tumor size (≤ 1 cm, > 1-2 cm, > 2 cm), estrogen receptor status (positive/negative), and node status (positive/negative); and 4) patient-physician interactions associated with treatment decision-making: patients' perceptions of doctor-patient communication and ratings of their physicians' technical and interpersonal care, patients'

perceptions of their own abilities to communicate with their physicians, and the number times breast cancer specialists discussed treatment options. This latter variable was the sum of affirmative responses to the question: "Did _____ discuss options for your breast cancer treatment with you?". This question was asked in relation to all breast cancer specialists that the patient had consulted, including surgeons (also second opinions), medical oncologists, and radiation oncologists. Finally, we asked whether family members were involved in the treatment decision-making process.

The bivariate relationships between the four categories of independent variables and standard primary tumor therapy are displayed in Table 3. Age, marital status, education, physical function, tumor size, node status, and the number of times breast cancer specialists discussed treatment options were significantly associated ($p<0.05$) with the type of primary tumor therapy received. Older women, those who were not married, those with less education, those with poorer physical function, those with smaller tumors, those with negative nodes, and those with whom treatment options were discussed less frequently were less likely to receive standard primary tumor therapy.

In a multiple logistic regression model (Table 4) that controlled for tumor size, node status, comorbidity, and physical function, the patients' age, marital status, and the number of times breast cancer specialists discussed treatment options were significantly associated with the receipt of standard primary tumor therapy: modified radical mastectomy or the combination of breast conserving surgery, axillary dissection, and radiation therapy. Older women, women who were not married, and women with whom treatment options were discussed less frequently were less likely to receive standard primary tumor therapy.

In an attempt to understand whether patient preferences were the reasons why age and marital status remained significant predictors of primary tumor therapy after statistical control for such potentially important confounders as tumor size, comorbidity, and physical function, we performed a series of bivariate analyses, relating patients' age and marital status to factors identified by them as being important in their decision-making about their breast cancer treatment. With respect to age, the only issue of differing importance by age was whether women had other responsibilities, such as caring for other family members. About 20% of women in both the 55-64 and 65-74 year old groups indicated that this was a *very important* consideration, whereas only 7% of the ≥ 75 year old group indicated that it was *very important* ($p<0.01$). In fact, 83% of the ≥ 75 year old group indicated that this consideration was *not important at all*. All women, regardless of age, reported that minimizing the possibility of recurrence was a *very important* consideration in their decision-making process.

Three factors related to marital status emerged as being important in women's treatment decision-making. Women who were not married were more likely to indicate that problems they would experience after surgery ($p<0.05$) and what they would have to pay over and above what their insurance would cover ($p<0.01$) were *very important* considerations in their treatment decision-making. In contrast, married women, as with younger women, reported that having other responsibilities was a *very important* consideration ($p<0.01$).

Experimental Methods Used for Current Study

Institutional Review Board Approval: All annual Institutional Review Board approvals were obtained from each of the study sites. We received approval from Faulkner Hospital on November 14, 1995; from Boston Medical Center on November 15, 1995; from Boston City Hospital on December 27, 1995; from Beth Israel Hospital on October 16, 1995; and from New England Medical Center on December 12, 1995. Approvals are updated annually.

Study Implementation

Subject Enrollment and First Follow-up Interview in the Current Study. Subjects enrolled in the NCI study are mailed a consent packet 20 months after their diagnosis date. This time interval was chosen because it was the shortest interval from initial diagnosis possible with the initiation of the US Army Research, Development, Acquisition and Logistics Command funding. To date, 297 of the 302 patients from the cohort have been contacted to participate in the present study and 249 have completed their first follow-up interview. The non-participation rate is 16%. Twenty-four patients could not be contacted because of changes in telephone numbers or addresses, or summer travel. An additional six patients had died and two were too ill to participate. Only 16 patients (5%) actually refused to participate. We will continue to enroll subject participants from the NCI project until all have reached 20 months of follow-up.

Second Follow-up Interview. Our second follow-up interview occurs approximately 12 months after the first follow-up interview. To date, 187 subjects have completed their second follow-up interview. A total of 32 (16%) have not participated. Fourteen could not be reached because residence and telephone numbers had changed. Seven patients had died and two were too ill to participate. Only 3 (2%) refused to participate.

Third Follow-up Interview. Our third follow-up interview occurs approximately 12 months after the second follow-up interview. To date, 59 subjects have completed their third and final follow-up interview. A total of 16 (25%) have not participated. Ten could not be reached because residence and telephone numbers had changes. Five had died and one was too ill to participate. No one refused to participate.

Collection of Surveillance Data. Medical record abstractions began in November 1994, and additional medical record abstractions are performed annually for each participant. To assess inter-rater reliability, a 20% random sample of charts are reviewed by Dr. Silliman.

To date, medical record abstractions have been completed for 229 of the 249 (92%) of subjects who have completed the first follow-up interview; 151 of the 187 (81%) of subjects who have completed the second follow-up interview; and 43 of the 59 subjects (73%) who have completed the third follow-up interview.

Preliminary Results for Current Study

Factors Associated with the Receipt of Systemic Adjuvant Therapy (analyses of baseline interview and medical record data and follow-up medical record data).

About two-thirds of the women studied received some form of systemic adjuvant therapy (Table 2). Bivariate relationships between the four categories of independent variables described

above in relation to standard primary tumor therapy and systemic adjuvant therapy are displayed in Table 5. Age, tumor size, estrogen receptor status, node status, the number of times treatment options were discussed, and whether or not patients' family members participated in the treatment decision-making process were significantly associated with the type of systemic adjuvant therapy received (all $p<0.05$).

In a multiple logistic regression model that controlled for tumor size, node status, estrogen receptor status, comorbidity, physical function, and primary tumor therapy, whether patients' family members participated in the treatment-decision making process and the number of times treatment options were discussed were significantly associated with the receipt of systemic adjuvant therapy (Table 6). Women who did not have family members involved in the treatment decision-making process and women who with whom treatment options were discussed less frequently were less likely to receive systemic adjuvant therapy.

First Follow-Up Interview.

Our first follow-up interview which is completed approximately 21 months after the date of diagnosis, focuses on adjuvant therapy and follow-up care. Preliminary results reflect 249 women who have completed their first follow-up interviews.

Systemic Adjuvant Therapy. Sixty-seven percent of patients (n=164) reported that their physicians had recommended adjuvant tamoxifen therapy and 94% (n=154) of these women reported that they had actually begun tamoxifen therapy. Of the 154 patients who had taken tamoxifen at any time, 85 (55%) reported that they had experienced side effects. Table 7 shows the type of side effects experienced by the women. The most common side effect reported was hot flashes, which were experienced by 74% of the women. Vaginitis and depression were two other side effects reported by an important minority of patients. Nonetheless, at the time of the interview, 137 patients (89%) reported that they were still taking tamoxifen.

Only 43 (18%) patients reported that adjuvant chemotherapy was recommended, and all but one of these patients received treatment. Most (39 of 42) patients who began chemotherapy reported that they experienced side effects. Tables 8 shows the type of sides effects experienced by these patients. The two most commonly reported side effects, each reported by over 90% of the women, were hair loss and fatigue; 85% of women reported that they were troubled by nausea. However, only four patients did not complete a complete course of therapy.

Follow-up Care. Our subjects reported that they saw their family physicians about two times in the previous year (mean=2.2), on average. The mean number of visits per year to their breast cancer surgeon was 1.8. The mean number of visits to their medical oncologist was 1.6. Finally, for radiation oncologist visits, the mean number of visits were 1.1. Approximately 60% of women reported that they felt calm before their breast cancer-related visits, while 27% reported that they did not. Similarly, 19% of women reported that they felt upset before their visit, while 71% stated that they did not. The vast majority of women reported that they felt good after a visit with their breast cancer specialist. Only 3% of women stated that they felt scared after a visit; 95% reported that they felt confident. Future analyses using medical record abstract data will allow us to determine whether it is abnormal test results, referrals for further testing, or the detection of recurrence that explain why a few patients feel upset after their visits and,

conversely, whether the vast majority leave feeling better because they have been declared disease free.

Patients were asked how they felt they were doing with worries and feelings surrounding their cancer. Most women, almost two years beyond their breast care diagnosis, reported that they feel they are doing well managing long-term life concerns. More than half of the patients (59%) felt they were doing excellent or very good with dealing with feelings of anger, fear and grief. Similarly, over half of the patients felt they were doing excellent or very good with their worries regarding their family's ability to manage if they got sicker, or worries about who would take care of them if they got sicker (53% and 48% respectively). However, approximately 16% of patients did not feel they were doing well with worries about recurrence of cancer.

First Follow-up Medical Record Surveillance.

As noted above, medical record abstractions have been completed for 229 (92%) of the 249 subjects who have completed their first follow-up interview. During the first surveillance period (between 6 and 18 months following diagnosis), subjects were seen up to seven times by surgeons, radiation oncologists, and medical oncologists. The average number of visits during this year was 2.0 for surgeons, 1.2 for radiation oncologists, and 1.2 for medical oncologists. Note that these figures are not dissimilar in comparison to the self-report data from the first follow-up interview (see above). These women averaged 4.4 visits to breast cancer specialists during their first surveillance year. During that year they had up to five mammograms (21% had none; the average was (1.6) and up to six carcinoembryonic antigen (CEA) tests (68% had none; the average was (0.7). Ten women developed recurrences, five of whom were 75 years of age or older.

Preliminary Analyses Combining Baseline and First Follow-up Interview and Medical Record Data.

Predictors of Outcomes at Twenty-one Months of Follow-up. We have conducted preliminary analyses examining the relationships among baseline patient characteristics, follow-up care, and general and breast cancer-specific quality of life at 21 months. With general emotional health at twenty-one months as the outcome variable and controlling for age, statistically significant predictors include marital status and attendance at religious services at baseline, and follow-up ratings of physicians' technical and interpersonal care and ratings of patients' own abilities to give to and to get the information that they need from their physicians (all $p < 0.05$). With breast-cancer specific worries as the dependent variable, follow-up ratings of physicians' technical and interpersonal care and ratings of patients' own abilities to give to and to get the information that they need from their physicians were the only statistically significant variables. Finally, age and attendance at religious services were the only two independent predictors of physical function at follow-up. Total number of visits to breast cancer specialists was not statistically significant in any of the models.

Second Follow-Up Interview.

Our second follow-up interview occurs approximately 12 months after the first interview and includes much of the same information as the first follow-up interview. In addition, it asks more specific questions about adjuvant tamoxifen therapy and gynecological surveillance and evaluation. We added these latter questions because of the concern about endometrial cancer risk and the uncertainty regarding the value of screening in this setting. To date, 187 subjects have completed their second follow-up interview.

Adjuvant tamoxifen therapy and gynecological care. Sixty-five percent (n=121) reported that they had been prescribed tamoxifen. Of the current tamoxifen users (n=99), 48% reported experiencing side effects. The most common side effects were hot flashes (62%), vaginitis (13%), and depression (13%). In addition, 26 patients complained of 22 other side effects that they attributed to tamoxifen.

We asked patients who had ever taken tamoxifen if they were referred to a gynecologist. Of the 116 who responded, 23% had been referred to a gynecologist once they started using tamoxifen. For patients who received gynecological care, 16% had had a vaginal ultrasound, and 11% had had an endometrial biopsy.

Emotional Adjustment. Patients were asked how they felt they were doing with worries and feelings surrounding their cancer. More than half of the patients (61%) felt they were doing excellent or very good with dealing with feelings of anger, fear and grief. Similarly, over half of the patients felt they were doing excellent or very good with their worries regarding their family's ability to manage if they got sicker, or worries about who would take care of them if they got sicker (55% and 50% respectively). However, approximately 19% of patients did not feel they were doing well with worries about recurrence of cancer. Nonetheless, after asking patients to respond to certain statements about how they were feeling about their lives, 80% responded they "enjoyed life", 88% had "accepted their illness", and 73% were "content with their quality of life". Of note, 25% of patients were concerned about the risk of cancer in their family members.

Third Follow-up Interview.

Our third follow-up interview is a subset of questions from the second follow-up interview. Questions that no longer pertain to patients three years after their primary treatment have been dropped, and in addition we will be asking more in depth questions about long term side-effects from surgery and radiation therapy. A total of 59 women have completed their third and final interview.

Long-term side-effects. By the time of the third interview (approximately 44 months after diagnosis), 15% reported that it was *somewhat* or *very difficult* to push or pull large objects, 19% reported difficulty extending their arms over their head, and 25% reported that it was difficult to lift items over 10 pounds. In addition, 25% reported persistent swelling or other difficulties with the arm on the side of their surgery and 31% reported persistent numbness or pain in the axilla.

Mortality. As of this writing, twenty-two subjects have died (7%). We have obtained death certificates for fourteen of these. Ten (71%) died of breast cancer, two (14%) died of other malignancies (lymphoma and multiple myeloma), and one each died of septic shock and a myocardial infarction. Women in this study do not appear to be dying of competing comorbid causes.

Plans for the 04 Project Year.

All of our first follow-up interviews will be completed during the 04 Project Year and second and third follow-up interviews will be completed as they become due. However, all second and third follow-up interviews will not be completed during the 04 Year. Because of the long period of time required to enroll the cohort, the time to complete full follow-up for each subject is equally long. We have requested a two year extension of the project so that we can obtain complete follow-up for all subjects (see Appendix A for Letter of Request).

Medical record abstracting will continue throughout the 04 Year. Each subject has a medical record abstract form related to each year of follow-up after the completion of her initial definitive treatment. Medical abstracting ends if patients develop metastatic disease or die. If patients develop in-breast recurrence or contralateral disease, abstracting is suspended until the second episode of definitive treatment has been completed. For each subject, medical record abstracting continues until the four year anniversary date of her initial treatment. To date, medical record abstracting has been completed on 43 subjects. For patients who have died, we will continue to obtain copies of death certificates from the Massachusetts Department of Health to determine the immediate and underlying causes of death.

7. CONCLUSIONS

Because the current project is as yet not complete, we cannot comment regarding project implications. However, it is important to note that several products have emanated thus far from the combination of the parent study and the current study.

1) Dr. Silliman (Principal Investigator) and colleagues submitted a grant proposal to the National Cancer Institute June 1, 1995 entitled "Adjuvant Tamoxifen Therapy in Old Age: Determinants and Consequences" (R01 CA/AG 70818). It was funded and began September 30, 1996.

2) Dr. Silliman was invited to write an editorial as a companion to an article on age-related treatment variations published in the Journal of the National Cancer Institute June 4, 1996.

3) Two manuscripts have been submitted for publication (see Appendix B for copies of these manuscripts):

a. Silliman RA, Troyan SL, Guadagnoli E, Kaplan SH, Greenfield S. The impact of age, marital status, and physician-patient interactions on the care of older women with breast cancer. Cancer 1997; in press.

b. Silliman RA, Prout MN, Field T, Kalish SC, Colton T. Risk factors for a decline in upper body function following therapy for early stage breast cancer. J Clin Oncol (Under Review).

4) Dr. Silliman has co-authored two book chapters with Dr. Lodovico Balducci:

a. Silliman RA, Balducci L. Breast cancer. In: L Balducci, GH Lyman, WB Ershler, eds: Geriatric Oncology (2nd ed). Philadelphia: JB Lippincott Company, in press.

b. Silliman RA, Balducci L. Breast cancer. In: Gallo J, Busby-Whitehead J, Rabins P, Silliman R, Murphy J: Reichel's Care of the Elderly: Clinical Aspects of Aging (5th ed). Baltimore: Williams & Wilkins, in press.

5) Dr. Silliman was invited to speak at the Cancer in the Elderly 1996 Conference (November 1996), at a lecture series sponsored by the Massachusetts Department of Health (January 1997), and at a special meeting of medical oncology educators in Puerto Rico (February 1997).

6) Dr. Silliman has been invited to participate in a two and one-half day retreat to assist the National Cancer Institute's Breast Cancer Progress Review Group (September 1997).

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Table 1. Patient Demographics and Clinical Characteristics (n=302)*

Characteristic	n (%)
Demographics	
Age	
55-64	123 (41)
65-74	111 (37)
75+	65 (22)
Race	
White	280 (94)
African-American	13 (4)
Other Minority	7 (2)
Marital Status	
Married	148 (49)
Widowed	98 (33)
Single	23 (8)
Divorced/Separated	30 (10)
Education	
< High School	51 (17)
High School Graduate	107 (36)
> High School	141 (47)
Health Status	
Comorbidity (mean ± SD)	7.06 ± 2.4
Physical Function (mean ± SD)	73.75 ± 21.61
Tumor Characteristics	
Histology	
Infiltrating Ductal	259 (86)
Infiltrating Lobular	31 (10)
Other	12 (4)
Tumor Size	
≤1 cm	85 (31)
>1 - 2 cm	128 (46)
>2 cm	65 (23)
Node Status	
Negative	241 (80)
Positive	60 (20)
Estrogen Receptor Status	
Positive	209 (76)
Negative	67 (24)

* All categories do not add up to 302 due to missing values

Table 2. Breast Cancer Therapy (n=302)*

	n (%)
Primary Tumor Therapy	
Breast Conserving Surgery/Radiation	169 (56)
Modified Radical Mastectomy	65 (21)
Other	68 (23)
Systematic Adjuvant Therapy	
Chemotherapy Alone	27 (9)
Chemo/hormonal Therapy	22 (7)
Hormonal Therapy Alone	154 (51)
None	99 (33)

* All categories do not add up to 302 due to missing values

Table 3. Factors Associated with Primary Tumor Therapy (n=302)

Factors	Modified Radical Mastectomy	Breast Conserving Surgery/Radiation Therapy	Other
Demographics [n, %]			
Age*			
55 - 64	34 (28)	77 (62)	12 (10)
64 - 74	20 (18)	73 (66)	18 (16)
75 +	11 (17)	17 (26)	37 (57)
Marital Status*			
Married	37 (25)	93 (63)	18 (12)
Not Married	28 (19)	75 (49)	49 (32)
Education*			
< High School	8 (16)	22 (43)	21 (41)
≥ High School	57 (23)	146 (59)	45 (18)
Health Status [mean score]			
Comorbidity	6.91	7.03	7.27
Physical Function*	72.46	76.69	67.22
Tumor Characteristics [n, %]			
Tumor Size*			
≤1 cm	8 (9)	53 (62)	24 (28)
>1 - 2 cm	16 (12)	79 (62)	33 (26)
>2 cm	29 (45)	29 (45)	7 (10)
Estrogen Receptor Status			
Positive	42 (20)	122 (58)	45 (22)
Negative	19 (28)	37 (55)	11 (17)
Node Status*			
Negative	43 (18)	134 (56)	64 (26)
Positive	22 (37)	35 (58)	3 (5)
Patient-Physician Interactions [mean score]			
Doctor-Patient Communication	93.17	92.05	92.19
Technical and Interpersonal Care	95.29	94.90	96.15
Perceptions of Abilities to Communicate	71.28	71.90	67.76
Times Treatment Options Discussed*	2.6	2.23	2.1
Family Member Participation in Treatment [n, %] Decision-Making			
Yes	21 (23)	57 (64)	12 (13)
No	44 (21)	112 (55)	50 (24)

* $p < 0.05$

Table 4. Multiple Logistic Regression Model Predicting Receipt of Standard Primary Tumor Therapy*

Variable	β Coefficient	Odds Ratio (95% CI)
Tumor Size		
≤ 1 cm (referent)	--------	----------
> 1-2	0.2948	1.34 (0.62, 2.89)
> 2	1.5372	4.65 (1.48, 14.65)
Node Status (positive/negative)	1.3265	3.77 (1.02, 13.95)
Age Group		
55 - 64 years	2.3032	10.01 (3.78, 26.47)
65 - 74	1.8580	6.41 (2.68, 15.35)
75+ (referent)	--------	----------
Marital Status (married/not)	0.8961	2.45 (1.17, 5.15)
Times Treatment Options Discussed (continuous)	0.5423	1.72 (1.14, 2.61)

* Adjusted for comorbidity and physical function

Table 5. Factors Associated with Systemic Adjuvant Therapy (n=302)

actors	Chemotherapy	Chemo/Hormonal Therapy	Hormonal	None
atient Demographics [n, %]				
Age*				
55-64	21 (17)	15 (12)	48 (39)	39 (32)
65-74	6 (5)	6 (5)	63 (57)	36 (33)
75 +	0 (0)	1 (2)	41 (63)	23 (35)
Marital Status				
Married	16 (11)	12 (8)	70 (47)	50 (34)
Not Married	11 (7)	10 (7)	82 (54)	49 (32)
Education				
< High School	4 (8)	1 (2)	26 (51)	20 (39)
≥ High School	23 (9)	21 (9)	125 (50)	79 (32)
ealth Status [mean score]				
Comorbidity	6.65	6.55	7.2	7.1
Physical Function	77.78	76.82	72.30	74.18
umor Characteristics [n, %]				
Tumor Size*				
≤1 cm	4 (5)	2 (2)	34 (40)	45 (53)
>1 - 2 cm	10 (8)	10 (8)	72 (56)	36 (28)
>2 cm	11 (17)	9 (14)	34 (52)	11 (17)
Estrogen Receptor Status*				
Positive	8 (4)	14 (7)	127 (61)	60 (28)
Negative	18 (27)	7 (10)	18 (22)	24 (36)
Node Status*				
Negative	15 (6)	5 (2)	127 (53)	94 (39)
Positive	12 (20)	17 (28)	26 (43)	5 (9)
atient-Physician Interactions [mean score]				
Doctor-Patient Communication	99.44	89.77	92.23	92.46
Technical and Interpersonal Care	98.38	94.32	95.36	94.39
Perceptions of Abilities to Communicate	68.52	76.90	70.78	70.41
Times Treatment Options Discussed*	2.67	2.55	2.5	2.21
Family Member Participation in Treatment Decision-Making [n, %]*				
Yes	16 (18)	7 (8)	47 (52)	20 (22)
No	11 (5)	15 (7)	102 (50)	78 (38)

$p < 0.05$

Table 6. Multiple Logistic Regression Model Predicting Receipt of Systemic Adjuvant Therapy*

Variable	β Coefficient	Odds Ratio (95% CI)
Tumor Size		
≤ 1 cm (referent)	--------	----------
> 1-2	0.7629	2.15 (1.11, 4.15)
> 2	1.4501	4.26 (1.74, 10.45)
Node Status (positive/negative)	1.8372	6.28 (2.05, 19.21)
Estrogen Receptor Status (positive/negative)	0.6559	1.93 (0.95, 3.91)
Family Help with Decision Making (yes/no)	0.7459	2.11 (1.08, 4.10)
Times Treatment Options Discussed (continuous)	0.4771	1.61 (1.12, 2.32)

* Adjusted for comorbidity, physical function, and primary tumor therapy

Table 7. Reported Side Effects of Tamoxifen Treatment (n=86)	
Type of Side Effect	**n (%)**
Hot flashes	64 (74)
Vaginitis	22 (26)
Depression	18 (21)
Nausea	8 (9)
Phlebitis	3 (4)
Edema	3 (4)
Other	35 (41)

Table 8. Reported Side Effects of Chemotherapy (n=42)	
Type of Side Effect	**n (%)**
Hair loss	36 (92)
Fatigue	37 (95)
Nausea	33 (85)
Depression	22 (56)
Flu Symptoms	17 (44)
Mouth Sores	13 (33)
Other	12 (31)

APPENDIX A

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18 July 1997

Susan Rupprecht/MCMR-AAA-B
US Army Medical Research Acquisition Activity
820 Chandler Street
Fort Detrick, Maryland 21702-5012

RE: DAMD17-94-J-4279

Dear Ms. Rupprecht:

We are writing at the suggestion of Dr. Modrow to request a two year extension of our project. In other words, we would like the project to end April 30, 2000 rather than April 30, 1998. The reasons are as follows. The accrual of our original cohort was slower than anticipated when we submitted our original proposal. Although we extended enrollment through April 1996, we were only able to recruit 302 women instead of our projected 350. Because enrollment extended over a long period, to obtain a full four years of follow-up on all subjects will require data collection to continue through December 1999. We would plan to use the remaining four months of the project for final data analysis and report writing.

Having a full four years of follow-up for all subjects is desirable for several reasons. First, it will maximize sample size and statistical power. Second, our preliminary results indicate that older women are very unlikely to die of non-cancer causes and most women are dying of their breast cancer. Furthermore, recurrences are more likely to occur in the group of women at highest risk for undertreatment (those $\geq$ 75 years of age). If these preliminary findings hold, they will provide new information about the outcomes of breast cancer care among older women. Finally, we have the unique opportunity to examine the relationships between initial and follow-up care and a range of patient outcomes (recurrence, death, and health-related quality of life). To our knowledge, this extensive a data collection effort (breadth and duration) has never been undertaken with a sample of older women.

Although we understand that there are no guarantees about additional funding in conjunction with the two year project extension, we are submitting a proposed budget and budget justification. We are confident that we can fund the second of the two years through internal funding sources, but request US Army Medical Research Command funding for the first year: $42,129. The budget projections are based on the need to conduct a total of 120 interviews and

medical record reviews. The assumptions underlying these projections are detailed in the budget justification.

As requested, we are including two additional copies of this letter, the budget, and the budget justification. Note that the grantee institution remains New England Medical Center, with the majority of the requested funds being in a subcontract to Boston Medical Center where the project is being conducted.

Yours sincerely,

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Boston Medical Center

Sherrie H. Kaplan, PhD
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James E. Grayson, Director
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APPENDIX B

Title Page

Manuscript Title: THE IMPACT OF AGE, MARITAL STATUS, AND PHYSICIAN-PATIENT INTERACTIONS ON THE CARE OF OLDER WOMEN WITH BREAST CANCER

Running Title: THE CARE OF OLDER WOMEN WITH BREAST CANCER

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Supported by Grants #RO1 CA57754 from the National Cancer Institute, National Institutes of Health and DAMD17-94-J-4279 from the US Army Research, Development, Acquisition and Logistics Command.

No portion of this manuscript has been published previously. However, findings in part were included in a presentation entitled "Patient-Physician Interactions" as part of an invited conference "Integrating Geriatrics into Oncology" held February 21-26, 1997 in Puerto Rico.

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Acknowledgments

We are grateful to the patients and physicians who participated in this study and for the thoughtful suggestions of Dr. Patricia A. Ganz who reviewed an earlier version of the manuscript.

Pages

Text: 24

Tables: 3

Precis

In the setting of newly diagnosed breast cancer in older women where there is clinical uncertainty as to the most appropriate therapies, patients may be better served by being offered choices among definitive therapies. In discussing therapies with them, physicians must be sensitive to their fears and concerns about the monetary costs and functional consequences of treatment in relation to expected benefits.

Abstract

Background: Understanding why older women with breast cancer do not receive definitive treatment is critical if we are to reduce disparities in mortality between younger and older women.

Methods: We studied 302 women ≥ 55 years of age with early stage breast cancer. Data were collected from surgical records and telephone interviews with the women. The main outcome was receipt of definitive primary tumor therapy, defined as either modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy.

Results: The majority (56%) of women underwent breast conserving surgery and axillary dissection followed by radiation therapy. After statistical control for comorbidity, physical function, tumor size, and node status, patients' age, marital status, and the number of times breast cancer specialists discussed treatment options were significantly associated with the receipt of definitive primary tumor therapy.

Conclusions: In the setting of newly diagnosed breast cancer in older women where there is clinical uncertainty as to the most appropriate therapies, patients may be better served by being offered choices among definitive therapies. In discussing therapies with them, physicians must be sensitive to their fears and concerns about the monetary costs and functional consequences of treatment in relation to expected benefits.

Key Terms: Breast cancer, early stage, treatment, aging, postmenopausal

Background

The cumulative risk for breast cancer reaches its maximum well into the ninth decade of life. Almost half of all newly diagnosed breast cancers occur in women who are 65 years of age or older (1). Although older women are less likely to die of their breast cancer than are younger women (2), recent evidence suggests that older women who do not receive definitive primary tumor therapy are at greater risk of dying from their breast cancer than are older women who do receive definitive therapy (3). This finding is particularly important because older women are also at greater risk of not receiving definitive treatment than are younger women (4-12).

Understanding the reasons why older women do not receive definitive treatment, particularly if the receipt of such treatment results in poorer patient outcomes, is critical if we are to improve such outcomes. Previous investigations have evaluated the potential roles of patients' health status [comorbidity and functional status] (6, 8, 11); patients' and their families' preferences and support (13, 14); and aspects of patient-physician interactions [physicians' attitudes and beliefs (8, 15) and the adequacy of patient-physician communication (16)] in explaining age-related treatment variations. For example, when tumor characteristics are taken into account, comorbidity and functional status do not completely explain the tendency for older women to receive less than definitive treatment (6, 8, 11). In addition, married women are more likely to receive definitive therapy than are their unmarried counterparts (10, 13). Finally, physicians who report a greater willingness to involve patients in treatment decision-making tend to be those who recommend breast conserving surgery without regard to age (15).

In addition to the well-known association, particularly among women, between older age and being unmarried (17), an emerging literature has documented that the quality of physician-

patient interactions decreases with patient age. Physicians tend to spend less time with their older patients than with their younger patients, and to be less respectful towards their older patients than towards their younger patients. For their part, older patients tend to be less assertive and to defer more to their physicians for treatment decisions than do their younger counterparts (18). Whether these features of patient-physician interactions represent cohort effects that will disappear with subsequent generations of physicians and patients is not known. For the present, however, they remain.

Because previous studies of age-related variations in breast cancer care have not evaluated comprehensively the extent to which patients' age, marital status, health status (comorbidity and functional status), tumor characteristics, and aspects of physician-patient interactions are independently associated with treatments received, we studied older women newly diagnosed with early stage breast cancer and identified factors associated with the receipt of definitive primary tumor therapy. We chose 55 years of age as the lower bound of age eligibility in order to have a group with which to compare the young old (65-74 years of age) and the older old (75+ years of age) age groups. We used a conservative definition of definitive primary tumor therapy (modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy), recognizing that there are no specific guidelines for the care of older women with early stage breast cancer.

Methods

Sampling:

Women ≥ 55 years of age, newly diagnosed with histologically confirmed stage I and stage II invasive breast carcinoma, who had no previous history of other kinds of cancer within the previous five years, no previous history of breast cancer, and who were cared for at one of five hospitals with academic affiliation in Boston, Massachusetts were eligible for study.

To identify potentially eligible patients, project staff reviewed pathology reports at each participating hospital on a regular basis, beginning in October 1992 and ending in December 1995. Names of potentially eligible patients were faxed to participating surgeons who confirmed eligibility and also indicated if there were any patients that he/she did not want us to contact and the reason for this decision. Eligible patients were sent an introductory letter signed by their surgeon and a consent form approximately two to three months following initial surgical treatment. This was followed by a telephone call from our interviewer who further explained the study, answered questions, and obtained informed consent.

Data Collection and Instrumentation:

Data were collected via a review of patients' surgical records and a computer-assisted telephone interview with consenting eligible patients.

Medical Record Abstract. Data collected from medical records included: histology (infiltrating ductal, infiltrating lobular, medullary, mucinous/colloid, or tubular), tumor size (largest diameter of the sum of the largest diameter of all fragments, stage (TNM), estrogen receptor status (positive or negative according to each laboratory's reference values), the results of axillary dissection if performed, breast surgery or surgeries performed (mastectomy or breast conserving

surgery), and additional therapies received (radiation therapy, chemo- and/or hormonal therapy). Because the performance of axillary dissection is related to age and we were particularly interested in patterns of care related to age, we chose not to exclude patients who could not be staged based on axillary node pathology. Such women were staged clinically.

Medical records were monitored for six months following surgery to determine whether radiation therapy and chemotherapy were initiated and completed, and whether hormonal therapy was initiated. All medical record information was collected by two trained research assistants. A 20% random sample of records abstracted by each research assistant was rereviewed by the other as well as by one of us (RAS). Item inter-rater reliabilities ranged from 88-100%, with most discrepancies occurring early in the study.

Patient Interview. The patient telephone interview was conducted an average of 4.5 months following patients' definitive surgery; it took 35 minutes to complete. It included questions about demographic characteristics (age, race, marital status, living arrangements, education, employment, and income); cardiopulmonary comorbidity and functional status; factors important in breast cancer treatment decision-making, including goals of therapy, side effects of treatment, recommendations of physicians, family, and friend, and cost; and perceptions of doctor-patient communication. All interviews were conducted by one experienced interviewer.

Major Analytic Variables: Our main outcome variable was definitive primary tumor therapy, defined as either modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy, versus all other primary therapies received (e.g. breast conserving surgery without radiation therapy).

For our independent variables we considered variables from four categories. First, we considered demographic characteristics, including age (categorized as 55-64, 65-74, 75+ to allow for comparisons among those in late middle age, the young old, and the older old), marital status (married/not married), and education (< high school/ ≥ high school). We did not include income because of the large amount of missing data (24% of subjects did not provide income information).

Second, we considered two measures of health status since comorbidity and functional status have been shown to contribute unique information to the understanding of the health of older persons (19, 20). We assessed comorbidity using a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease, and related disease manifestations and symptoms that were part of the Total Illness Burden Index (21). The Total Illness Burden Index includes measures of 15 different disease categories and has been shown to be significantly associated with measures of functional status as well as with disability days and the use of health services (21). We restricted our assessment of comorbidity to the three disease categories that assess cardiopulmonary disease because these categories reflect the conditions that are most likely to influence the choice of primary tumor therapy and because we wanted to minimize respondent burden. In the resultant comorbidity measure a positive score reflects above average comorbidity.

We assessed physical function using the 10-item physical function subscale of the 36-item short form Medical Outcomes Study functional status questionnaire (SF-36) which is scaled from 0-100 with a higher score indicating better function. The SF-36 measures eight health concepts including physical function and was developed to represent well-validated parent full-

length scales without loss of statistical precision. Results from the Medical Outcomes Study indicate that the physical function subscale is reliable and clinically valid (22).

Third, we considered tumor characteristics: tumor size ($\leq$ 1 cm, > 1-2 cm, > 2 cm), estrogen receptor status (positive/negative), and node status (positive/negative). Fourth, we considered patient-physician interactions associated with treatment decision-making: patients' perceptions of doctor-patient communication (a four-item measure that rates the quality of breast cancer information given patients by their physicians, as well as physicians' abilities to give information, discuss treatment options, and tailor treatments to patient needs [Cronbach's α = 0.92]); patients' ratings of their physicians' technical and interpersonal care (a four-item measure that rates physicians' personal manner, communication skills, technical skills, and overall care [Cronbach's α = 0.95]), and patients' perceptions of their own abilities to communicate with their physicians (a three-item measure that patients' assesses abilities to get and give information [Cronbach's α = 0.96]). We also asked women about the number times breast cancer specialists discussed treatment options. This latter variable was the sum of affirmative responses to the question: *"Did _____ discuss options for your breast cancer treatment with you?"*. This question was asked in relation to up to four breast cancer specialists that the patient had consulted, including surgeons (also second opinions), medical oncologists, and radiation oncologists. Affirmative responses ranged from 78% for radiation oncologists, to 83% for surgeons who performed the diagnostic biopsy (98% for second opinion surgeons), to 87% for medical oncologists. Finally, we asked whether family members were involved in the treatment decision-making process.

Analytic Strategy: Descriptive statistics were obtained for all study variables. We then performed a series of bivariate analyses, examining the relationships between each independent variables and the dependent variable, using two independent sample t-tests and chi-square tests as appropriate. Our bivariate analyses were performed using a three-level form of the dependent variable (radical mastectomy vs. breast conserving surgery/axillary dissection/radiation therapy vs. all other therapies) in order to better appreciate differences across these categories of primary tumor therapy.

In our multiple logistic regression analysis we used a two-level form of the variable (definitive primary tumor therapy vs. all others) for four major reasons: 1) the majority of our subjects underwent breast conserving surgery with axillary dissection followed by radiation therapy; 2) modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy have been demonstrated to be equivalent with respect to mortality (23); 3) as noted above, recent data suggest that older women who receive less than definitive treatment are more likely to die of their breast cancer than are older women who receive definitive treatment (3); and 4) logistic regression models with more than a two-level dependent variable are often difficult to interpret.

We took a conservative approach to developing our logistic regression model. Because of the importance of comorbidity, functional status, tumor size, and node status in clinical decision-making, we forced these variables into our model. We then used stepwise multiple logistic regression techniques with significance criterion of 0.05 for entry or removal from the model for all other variables identified as being statistically significant on bivariate analysis.

Finally, in an effort to understand the results of our logistic regression analysis, we also performed a series of exploratory bivariate analyses, relating patients' age and marital status to factors identified by them as being important in their decision-making about their breast cancer treatment.

Results

Study Sample:

Three hundred eighty-eight eligible patients were identified whose surgeons gave permission for contact. Of these, 302 (78%) agreed to participate. Reasons for non-participation included: patient refusal (n=40), inability to contact (n=25), ill health (n=13), and non-English speaking without an available person to translate (n=8). Non-participants were three years older, on average, than participants (71.2 vs. 68.4 years, p=0.01). Equal proportions of participants and non-participants had stage I (78%) and stage II (22%) disease, respectively. No other information about non-participants was available.

Patient characteristics are displayed in Table 1. A little over half of our subjects were ≥ 65 years of age (range 55-97 years) and most were white. Half were married; most of the remainder were widowed. The majority had a high school education or greater. Their average comorbidity score was 7.06 (range 3-20). The majority of patients had infiltrating ductal carcinoma and had stage I disease. Stage I patients tended to be slightly older than stage II patients (mean age = 68.9 vs. 66.6 years). In addition, older patients were more likely to be estrogen receptor positive (55-64: 72% vs. 65-74: 74% vs. 75+: 86%).

Treatment Priorities:

We asked our subjects about factors that were important in their decision-making. Factors rated *very important* by almost all patients (100% and 96%, respectively) were two: 1) minimizing the possibility of recurrence, and 2) their doctors' recommendations. Although there was less consensus, also *very important* to the majority were quality of life after treatment (77%) and their family's opinion (52%). A substantial minority also rated what they would have to pay

over and above what their insurance would cover and problems they would experience after surgery as *very important* (28% and 22%, respectively). In contrast, three treatment-related factors were rated as *not important at all* by the majority of patients: 1) effects of treatment on sexuality (83%), 2) difficulty getting to and from treatments (65%), and 3) effects of treatment on looks (63%).

Predictors of Definitive Primary Tumor Therapy:

In contrast to patterns of care observed elsewhere among older women with breast cancer (8, 10-12), the majority of women in our study underwent breast conserving surgery and axillary dissection followed by radiation therapy (Table 1). Less than a quarter received a modified radical mastectomy. The remaining quarter received: 1) breast conserving surgery and radiation therapy, but no axillary dissection (n=26), 2) breast conserving surgery and axillary dissection, but no radiation therapy (n=22), 3) breast conserving surgery alone (n=10), or 4) other (n=10), including radiation therapy only, incisional biopsy only, and simple mastectomy with or without radiation therapy.

The bivariate relationships between each of the independent variables and primary tumor therapy, categorized as modified radical mastectomy, breast conserving surgery with axillary dissection followed by radiation therapy, or other are displayed in Table 2. Age, marital status, education, physical function, tumor size, node status, and the number of times breast cancer specialists discussed treatment options were each significantly associated ($p<0.05$) with the type of primary tumor therapy received.

In order to understand the independent contributions of variables identified as being statistically significant on bivariate analysis, we developed a multiple logistic regression model

(Table 3) that controlled for comorbidity, physical function, tumor size, and node status. Patients' age, marital status, and the number of times breast cancer specialists discussed treatment options were independently and significantly associated with the receipt of definitive primary tumor therapy: modified radical mastectomy or the combination of breast conserving surgery, axillary dissection, and radiation therapy. Older women, women who were not married, and women with whom treatment options were discussed less frequently were less likely to receive definitive primary tumor therapy, after taking into account differences in health status and tumor characteristics.

In an attempt to understand whether patient preferences were the reasons why age and marital status remained significant predictors of primary tumor therapy after statistical control for such potentially important confounders as comorbidity, physical function, tumor size, and node status, we performed a series of bivariate analyses, relating patients' age and marital status to factors identified by them as being important in their decision-making about their breast cancer treatment. With respect to age, the only issue of differing importance by age was whether women had other responsibilities, such as caring for other family members. About 20% of women in both the 55-64 and 65-74 year old groups indicated that this was a *very important* consideration, whereas only 7% of the ≥ 75 year old group indicated that it was *very important* ($p<0.01$). In fact, 83% of the ≥ 75 year old group indicated that this consideration was *not important at all.*

Three factors related to marital status emerged as being important in women's treatment decision-making. Women who were not married were more likely to indicate that problems they would experience after surgery ($p<0.05$) and what they would have to pay over and above what

their insurance would cover ($p<0.01$) were *very important* considerations in their treatment decision-making. In contrast, married women, as with younger women, reported that having other responsibilities was a *very important* consideration ($p<0.01$).

Discussion and Conclusions

In this study of age-related variations in early stage breast cancer treatment in the 1990's, we have found that the majority (56%) of women underwent breast conserving surgery and axillary dissection followed by radiation therapy. This percentage is higher than that observed even in younger women (10, 12) and is in keeping with the fact that the Northeast has among the highest rates of breast conserving surgery in the United States, even among older women (25, 26). In addition, age as well as marital status and an indicator of patient-physician interactions (the extent to which breast cancer specialists discussed treatment options), were independently associated with the receipt of definitive primary tumor therapy received by older women with early stage breast cancer. These associations persisted after statistical control for comorbidity, physical function, and relevant tumor characteristics.

The inability of these latter factors to completely explain age-related treatment variations in breast cancer care is in agreement with the findings of other investigators but requires explanation (6, 8, 11, 24). It is possible, for example, that we inadequately controlled for variations in health status and tumor prognostic factors in our multiple logistic regression model. We relied on women's reports of cardiopulmonary diseases and symptoms for our measure of comorbidity and on their reports of physical limitations due to their health. However, recent studies from Europe have documented that older patients can accurately report whether or not they have cardiovascular disease (27, 28), and our measure of physical function has been used widely in studies of older persons and has been shown to be sensitive to low levels of morbidity (29, 30). Furthermore, in our study older women reported more comorbidity and poorer physical function than did younger women, as would be expected (Table 1). Finally, we performed an

additional multiple logistic regression analysis, excluding women 75 years of age or older with very small tumors (< 1 cm). In this analysis, age persisted as an independent predictor of definitive primary tumor therapy.

We believe that clinical uncertainty as to the most appropriate therapies for older women affords the best explanation for the age-related variations that we have observed. In particular, there is controversy about the necessity of axillary dissection, as well as of radiation therapy following breast conserving surgery among older women. Questions about axillary dissection relate to its diagnostic versus therapeutic value (31); questions about postoperative radiation therapy arise because it has not been demonstrated to affect survival rates and, in addition, may not be necessary to achieve acceptably low recurrence rates in older women (32-34). It is clear from our data and those of others that axillary dissection and radiation therapy are being used preferentially less often in older women than in younger women. Among our patients, adjuvant systemic therapy (usually tamoxifen) appears to have been substituted for these procedures in about two-thirds of women who did not receive standard primary therapy. Whether this substitution results in similar outcomes is not known definitively, although there is case-series evidence that suggests that this strategy may be appropriate for older women with T1 tumors (35, 36).

Our findings confirm and extend the work of previous investigators who have found that being unmarried is a risk factor for not receiving definitive therapy for breast cancer (10, 13). Our older unmarried women were more concerned than were married women about treatment-related problems that they might experience after surgery and the out-of-pocket costs of their care. Both of these concerns may have led them to choose less intense primary tumor therapy

regimens. Whether their surgeons tended to offer such regimens preferentially to them is not known.

In this regard, an important finding in our study was the influence of the extent to which treatment options were discussed on the primary tumor therapies received by older women. Others have found that older women are less likely to receive medical or radiation oncologist consultations (7, 37) and that being offered a choice is more strongly related to psychosocial outcomes than is type of treatment (38). We believe that if patients are offered choices and are encouraged to be involved in their care, the decisions that they and their physicians make may more closely reflect their own values and preferences. When they are not, the decisions made may more closely reflect the values and beliefs of their physicians. Here, clinical uncertainty (or biases) about what represents appropriate care may importantly influence physician-directed decisions.

Our findings are provocative, but they must be interpreted with the following limitations in mind. First, we studied the care of largely of white well-educated older women in clinical settings with academic affiliation in one geographic region (Boston, Massachusetts). Second, selection factors resulted in our studying younger members, on average, of the eligible patient population. However, we believe that studies of older and more diverse patient populations may find an even larger impact of age, marital status, and patient-physician interactions on outcomes than we did. Third, we relied on women's recall of events and treatment decision-making that had occurred several months previously. Details of physician visits and thought processes may have been forgotten or recalled imperfectly. It seems unlikely, however, that this should have occurred differentially across treatment groups. Finally, our measure of the extent to which

treatment options were discussed was based on counts of reported discussions rather than an actual measure of the depth and extent of discussions such as would be available from audio or videotaping, or direct observations.

With these limitations in mind, it is clear that additional studies are needed that focus on both the process and outcomes of care for older women with breast cancer and that such studies must take into account comorbidity, functional status, and tumor characteristics, and must link therapies received with the important clinical outcomes of functional status, breast cancer recurrence, and breast cancer-specific mortality. Such studies are particularly important since the most recent breast cancer mortality figures demonstrate a marked decline in mortality in all age groups except those 80 years of age or older. Furthermore, the mortality rate in those 70-79 years of age did not decline between 1991 and 1993, as it did in every younger age group (39).

It is noteworthy that we found that almost all of the women in this study reported that minimizing the possibility of recurrence and their doctors' recommendations were very important considerations in their treatment decision-making. Our older patients may therefore be better served by us recommending definitive therapies or recommending that they participate in clinical trials and/or observational studies designed to answer the critical questions of treatment efficacy and effectiveness in older persons. In discussing therapies with them, we must be sensitive to their fears and concerns about the monetary costs and functional consequences of treatment in relation to expected benefits.

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Table 1. Patient Demographics and Clinical Characteristics (n=302)*

Characteristic	n (%)
Demographics	
Age	
55-64	123 (41)
65-74	111 (37)
75+	65 (22)
Race	
White	280 (94)
African-American	13 (4)
Other Minority	7 (2)
Marital Status	
Married	148 (49)
Widowed	98 (33)
Single	23 (8)
Divorced/Separated	30 (10)
Education	
< High School	51 (17)
High School Graduate	107 (36)
> High School	141 (47)
Health Status	
Comorbidity (mean ± SD)	7.06 ± 2.4
Physical Function (mean ± SD)	73.75 ± 21.61

* All categories do not add up to 302 due to missing values

Table 1. Patient Demographics and Clinical Characteristics (n=302)* Cont'd

Characteristic	n (%)
Tumor Characteristics	
Histology	
Infiltrating Ductal	259 (86)
Infiltrating Lobular	31 (10)
Other	12 (4)
Tumor Size	
≤1 cm	85 (31)
>1 - 2 cm	128 (46)
>2 cm	65 (23)
Node Status	
Negative	241 (80)
Positive	60 (20)
Estrogen Receptor Status	
Positive	209 (76)
Negative	67 (24)
Primary Tumor Therapy	
Breast Conserving Surgery/Axillary Dissection/Radiation Therapy	169 (56)
Modified Radical Mastectomy	65 (21)
Other	
Breast Conserving Surgery/Radiation	26 (9)
Breast Conserving Surgery/Axillary Dissection	22 (7)
	10 (3)
Breast Conserving Surgery Alone	10 (3)
Miscellaneous	

* All categories do not add up to 302 due to missing values

Table 2. Factors Associated with Primary Tumor Therapy (n=302)

Factors	Modified Radical Mastectomy	Breast Conserving Surgery/Radiation Therapy	Other
Demographics [n, %]			
Age*			
55 - 64	34 (28)	77 (62)	12 (10)
64 - 74	20 (18)	73 (66)	18 (16)
75 +	11 (17)	17 (26)	37 (57)
Marital Status*			
Married	37 (25)	93 (63)	18 (12)
Not Married	28 (19)	75 (49)	49 (32)
Education*			
< High School	8 (16)	22 (43)	21 (41)
≥ High School	57 (23)	146 (59)	45 (18)
Health Status [mean score]			
Comorbidity	6.91	7.03	7.27
Physical Function*	72.46	76.69	67.22
Tumor Characteristics [n, %]			
Tumor Size*			
≤1 cm	8 (9)	53 (62)	24 (28)
>1 - 2 cm	16 (12)	79 (62)	33 (26)
>2 cm	29 (45)	29 (45)	7 (10)
Estrogen Receptor Status			
Positive	42 (20)	122 (58)	45 (22)
Negative	19 (28)	37 (55)	11 (17)
Node Status*			
Negative	43 (18)	134 (56)	64 (26)
Positive	22 (37)	35 (58)	3 (5)
Patient-Physician Interactions [mean score]			
Doctor-Patient Communication	93.17	92.05	92.19
Technical and Interpersonal Care	95.29	94.90	96.15
Perceptions of Abilities to Communicate	71.28	71.90	67.76
Times Treatment Options Discussed*	2.6	2.23	2.1
Family Member Participation in Treatment [n, %] Decision-Making			
Yes	21 (23)	57 (64)	12 (13)
No	44 (21)	112 (55)	50 (24)

* $p < 0.05$

Table 3. Multiple Logistic Regression Model Predicting Receipt of Definitive Primary Tumor Therapy*

Variable	β Coefficient	Odds Ratio (95% CI)
Tumor Size		
≤ 1 cm (referent)	--------	----------
> 1-2	0.2948	1.34 (0.62, 2.89)
> 2	1.5372	4.65 (1.48, 14.65)
Node Status (positive/negative)	1.3265	3.77 (1.02, 13.95)
Age Group		
55 - 64 years	2.3032	10.01 (3.78, 26.47)
65 - 74	1.8580	6.41 (2.68, 15.35)
75+ (referent)	--------	----------
Marital Status (married/not married)	0.8961	2.45 (1.17, 5.15)
Times Treatment Options Discussed (continuous)	0.5423	1.72 (1.14, 2.61)

* Adjusted for comorbidity and physical function

RISK FACTORS FOR A DECLINE IN UPPER BODY FUNCTION FOLLOWING THERAPY FOR EARLY STAGE BREAST CANCER

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Supported by Grants #RO1 CA57754 from the National Cancer Institute, National Institutes of Health and DAMD17-94-J-4279 from the US Army Research, Development, Acquisition and Logistics Command.

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Running Head: Upper Body Function and Breast Cancer Therapy

Abstract

Purpose: To identify risk factors for a decline in upper body function following treatment for early stage breast cancer.

Methods: We conducted a cross-sectional observational study of 215 women ≥ 55 years of age newly diagnosed with early stage breast cancer interviewed three to five months following their definitive surgery. Patients were classified as having impaired upper body function related to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function (pushing or pulling large objects; lifting objects weighing more than 10 pounds; and reaching or extending arms above shoulder level) prior to treatment, but reported that any of these tasks were *somewhat* or *very* difficult in the four weeks prior to interview, or 2) they reported that performing any of the three tasks requiring upper body function was *somewhat* difficult prior to treatment, but reported that any of these tasks were *very* difficult in the four weeks prior to interview.

Results: In multiple logistic regression models, both the extent and type of primary tumor therapy and cardiopulmonary comorbidity were statistically significant independent predictors of a decline in upper body function following breast cancer treatment.

Conclusion: Given the critical importance of upper body function in maintaining independent living, clinicians should consider the functional consequences of treatment when they discuss treatment options and post-operative care with older women who have early stage breast cancer.

Introduction

Breast cancer has become increasingly common among older women. The incidence of breast cancer increases with age until at least the ninth decade of life, the number of older women at-risk has increased, and the age-adjusted incidence has increased, in part due to increased use of screening mammography (1). Furthermore, the increasing use of screening mammography has resulted in a greater proportion of older women being diagnosed with early stage disease (2). Earlier diagnosis, coupled with an overall increase in longevity in late life, will likely result in an increase in the number of older women who are long-term survivors of breast cancer. For these women, the functional consequences of breast cancer treatment, manifested in tasks that require upper body strength, are likely to assume greater importance, particularly as they concomitantly acquire age-related disabilities.

Satariano and colleagues studied the functional consequences of breast cancer therapy and found that among women ages 55-74 who were treated for breast cancer, at three months following diagnosis they were more likely than controls without breast cancer to report difficulty in completing tasks that required upper body strength (3). In another study by the same investigative team, analyses conducted with the case group failed to find a treatment effect. However, the treatment measure categorized radiation, chemotherapy, and hormonal therapy together as "adjuvant therapy". Thus, it was not possible to evaluate the effects of standard therapies nor of the specific components of these therapies on upper body function (4).

Because tasks that require upper body strength are crucial for maintaining independence, it is important to identify risk factors for breast cancer patients' decline in abilities to perform such tasks. Knowledge of these risk factors may aid in the identification of women at high risk for poor functional outcomes and in the choice of their primary breast cancer treatment.

We therefore conducted a cross-sectional study of women ≥ 55 years of age at three to five months after their treatment for newly diagnosed stage I and stage II breast cancer to identify risk factors for a decline in upper body functional abilities in relation to treatments received.

Methods

Sampling

Details of the study have been described elsewhere (5). In brief, we studied women ≥ 55 years of age, newly diagnosed with histologically confirmed stage I and stage II invasive breast carcinoma cared for at one of five hospitals in Boston, Massachusetts. Potential study participants were sent an introductory letter signed by their surgeon and a consent form at approximately two to three months following their definitive surgical treatment. An interviewer followed-up with a telephone call to explain the study further, to answer questions, and to obtain informed consent. We restricted the analyses described herein to those women interviewed three to five months following their definitive surgery to minimize variation associated with differing lengths of recovery time.

Data Collection

Data were collected via a review of patients' surgical records and a 35 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), and whether or not the patient received a course of post-operative radiation therapy. The patient telephone interview included questions about tasks that required upper body function and were asked in relation to breast cancer treatment: 1) pushing or pulling large objects, such as a living room chair, 2) lifting objects weighing more than 10 pounds, such as a heavy bag of groceries, and 3) reaching or extending arms above shoulder level. For each task, the subject was asked about its difficulty (*very, somewhat, or not difficult*) in performance during four weeks preceding interview as well as prior to their breast cancer treatment. These items were selected from the

items used by Satariano and colleagues (3), fielded previously in the Framingham Disability Study (6) and derived from the original work of Nagi (7). In addition, we asked questions about cardiopulmonary comorbidities that were part of the Total Illness Burden Index (8), as well as about demographic characteristics (age, race, marital status, education, height, and weight).

Major Analytic Variables

Our dependent variable was a decline in upper body function in relation to breast cancer treatment. Patients were classified as having a decline in upper body function in relation to their breast cancer treatment if: 1) they reported having no difficulty in performing any of the three tasks requiring upper body function prior to treatment, but reported that any of these tasks were *somewhat* or *very* difficult in the four weeks prior to interview, or 2) they reported that performing any of the three tasks requiring upper body function was *somewhat* difficult prior to treatment, but reported that any of these tasks were *very* difficult in the past four weeks.

For our independent variables we considered: age (55-64, 65-74, 75+) and education (< high school/≥ high school). We also considered body mass index (BMI: weight in kilograms divided by height in meters squared); comorbidity (a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related symptoms, with a positive score reflecting above average comorbidity); breast cancer characteristics, including tumor size (≤ 1 cm, >1-2 cm, > 2 cm) and node status (positive/negative); and breast cancer treatments received. For the breast cancer treatments variables, we used two different approaches. First, we considered each of the two standard treatments (modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy) in comparison to other primary therapies received (e.g. breast conserving surgery without radiation therapy). Second, we considered the specific

components of primary tumor therapy (axillary dissection, definitive surgery [mastectomy vs. breast conserving surgery], and radiation therapy).

Analytic Strategy

We obtained descriptive statistics for all study variables. We then performed a series of bivariate analyses, examining the relationships between independent variables and the dependent variable, using independent samples t-tests and chi-square tests as appropriate. Next, we developed multiple logistic regression models whose independent variables included all the statistically significant associations ($p < 0.05$) found in bivariate analyses, as well as all breast cancer treatment variables. We used stepwise multiple logistic regression techniques with significance criterion of 0.1 for entry or removal from the model.

Results

Two hundred fifteen women (71%) from the original cohort were interviewed three to five months following their definitive surgery and served as the study sample for this analysis. Sample characteristics are similar to those of the full cohort (5). Almost two-thirds (59%) were ≥ 65 years of age. Most were white (95%) and had a high school education or greater (84%). Half were married; most of the remainder were widowed. The average BMI was 25.98 (± 5.05) and the average comorbidity score was 7.09 (range 3-20). Most patients had small tumors (77% ≤ 2 cm) and were node negative (80%). The majority (57%) had undergone breast conserving surgery with axillary dissection followed by radiation therapy; 23% had undergone modified radical mastectomy. Of the 43 who received other than these standard primary tumor therapies, 23 underwent breast conserving surgery followed by radiation but without axillary dissection; 12 underwent breast conserving surgery and axillary dissection but did not receive radiation therapy; five underwent breast conserving surgery but neither axillary dissection nor radiation therapy; and the remainder either underwent simple mastectomy without radiation (n=2) or underwent biopsy or radiation therapy only (n=2). About a quarter of all subjects (27%) reported a decline in upper body function following their breast cancer treatment.

On bivariate analysis (Table 1), women who reported a decline in upper body function since breast cancer treatment had higher BMIs and cardiopulmonary comorbidity scores than those who did not report worsened upper body function, although only the comorbidity difference was statistically significant. In addition, women who received other than standard primary tumor therapies were about half as likely to report worsened upper body function as those who received either breast conserving surgery with axillary dissection and radiation therapy or a modified radical mastectomy (16% vs. 28% and 32%, $p = 0.18$). With respect to the

individual components of primary tumor therapy, women who underwent axillary dissection, mastectomy, or radiation therapy were all somewhat more likely to report a decline in upper body function since treatment than those who did not, but none of these relationships reached statistical significance.

In a multiple logistic regression model that included standard therapies (modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy), with non-standard primary tumor therapies as the referent group (Table 2, Model 1), women who received breast conserving surgery with axillary dissection and follow-up radiation therapy were 2.2 times more likely to report a decline in upper body function ($p=0.09$), and women who received modified radical mastectomy were 2.8 times more likely to experience a decline in upper body function ($p=0.05$). Cardiopulmonary comorbidity was also an independent predictor of a decline in upper body function ($p=0.02$). In a second multiple logistic regression model (Table 2, Model 2), women undergoing mastectomy or radiation therapy were each more than six times more likely to report a decline in upper body function than those who did not ($p=0.02$). As in Model 1, cardiopulmonary comorbidity also was an independent predictor of a decline in upper body function following breast cancer treatment ($p=0.04$).

Discussion

We have found that among older women with early stage breast cancer, the extent of primary tumor therapy, as well as specific components of therapy, and self-reported cardiopulmonary comorbidity are risk factors for a decline in upper body function during the early months following primary breast cancer therapy. To our knowledge, this is the first study to evaluate the both the early effects of different treatment regimens as well as comorbidity in a group of older women with early stage breast cancer.

Sneeuw and colleagues examined late functional outcomes (an average of four years after treatment) among women of various ages who received breast conserving surgery, axillary dissection, and radiation therapy. In this study from the Netherlands of 76 women (age range 37-75) who were treated between 1975 and 1985, nearly half of the subjects reported a little (34%) or moderate (13%) limitation of movement in the arm and shoulder on the treatment side (9). Gerber and colleagues compared functional outcomes among participants in a randomized clinical trial who received either modified radical mastectomy or breast conserving surgery with axillary dissection and follow-up radiation therapy. All subjects also participated in an extensive structured rehabilitation program. The average number of days to reach functional range of motion did not differ between the groups, but twice as many women who were treated in the breast conserving surgery treatment group reported chest wall tenderness one year after treatment, as compared to the women in the modified radical mastectomy treatment arm (58.4% vs. 27.4%, $p<0.0001$) (10). These data suggest that breast conserving surgery in conjunction with axillary dissection and radiation therapy may have substantial late functional consequences.

Our data are consistent with these investigations and extend those of Satariano and colleagues (3, 4). They demonstrate that there are early functional consequences among women

who receive either modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy, although the risk associated with modified radical mastectomy is greater. Furthermore, our treatment component-specific analyses suggest that it is the radiation therapy that is associated with an increased risk for women who undergo breast conserving surgery; axillary dissection does not appear to have an important influence.

Finally, cardiopulmonary comorbidity burden also is a risk factor for a decline in upper body function following primary tumor therapy. Tasks that require upper body strength stress the cardiopulmonary system. Thus, cardiopulmonary disease burden may limit rehabilitation efforts during the early treatment recovery period.

Of interest, the group of women at least risk for a decline in upper body function were those who received less than standard primary tumor therapy. It is therefore important to consider whether the offering of less intensive treatment may preserve upper body function at the expense of longer term survival. A recent study by Goodwin and colleagues has documented that older women who receive less than standard breast cancer therapy are at greater risk of dying from their breast cancer than those who receive standard therapy (11). Furthermore, recent breast cancer mortality trends document that breast cancer mortality has decreased in all age groups except the oldest old, who are also at greatest risk for receiving less than standard treatment (2). For many older women, the better short-term functional status associated with less intensive treatment may not offset the increased risk of breast cancer mortality.

Our findings must be considered with the study's major limitations in mind. First, we did not measure directly upper body function, either before or after treatment. Second, we did not gather side-specific information, either in relation to handedness or the side on which treatments were performed. Third, we did not collect information about prior recreational or occupational

injuries involving the upper extremities. Fourth, our sample was relatively small and the confidence intervals around our estimates of risk are wide. Nonetheless, our data are consistent with the limited number of studies to date and make clinical sense. Whether the early impairments that we have observed will persist awaits the collection of follow-up data.

Given the critical importance of upper body function in maintaining independent living (12), our findings suggest that clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with older women who have early stage breast cancer. In addition, we need to design studies to find the best balance between treatment efficacy and functional morbidity for this group of patients.

Acknowledgments

The authors thank Serkalem Demisse for assistance with statistical analysis and Timothy Lash for reviewing an earlier draft of this manuscript.

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Table 1. Bivariate Relationships between Patient Characteristics and Decline in Upper Body Function (n=215)

Characteristic	Declined (n=57)	Not Declined (n=127)	P Value
Demographic Characteristics			
Age (n , %)			
55-64	26 (30)	62 (70)	0.74
65-74	21 (25)	64 (75)	
75 +	10 (25)	30 (75)	
Education (n , %)			
< High School	10 (29)	25 (71)	0.81
≥ High School	47 (27)	130 (73)	
General Health Status (mean score)			
Body Mass Index (BMI)	26.93	25.63	0.15
Comorbidity	7.76	6.87	0.05
Breast Cancer Characteristics			
Tumor Size (n , %)			
≤ 1 cm	15 (25)	46 (75)	0.64
> 1 - 2 cm	23 (25)	69 (75)	
> 2 cm	15 (32)	32 (68)	
Node Status (n , %)			
Negative	44 (25)	127 (75)	0.71
Positive	12 (29)	30 (71)	
Breast Cancer Treatments			
Primary Tumor Therapy (n , %)			
Modified Radical Mastectomy	16 (32)	34 (68)	0.18
Breast Conserving Surgery/ Axillary Dissection/Radiation Therapy	34 (28)	87 (72)	
Other	7 (16)	36 (84)	
Specific Treatment Modalities (n , %)			
Axillary Dissection			
Yes	50 (27)	133 (73)	0.39
No	6 (20)	24 (80)	
Mastectomy			
Yes	16 (31)	36 (69)	0.42
No	40 (25)	120 (75)	
Radiation Therapy			
Yes	43 (29)	105 (71)	0.22
No	14 (21)	52 (79)	

Table 2. Multiple Logistic Regression Models Predicting A Decline in Upper Body Function in Relation to Breast Cancer Treatment

Characteristic	β Coefficient	Odds Ratio (95% CI)	
Model 1			
Primary Tumor Therapy			
Other (referent)	--------	----	
Breast Conserving Surgery	0.7678	2.2	(0.875, 5.53)
Modified Radical Mastectomy	1.0305	2.8	(1.002, 7.84)
Cardiopulmonary Comorbidity	0.1393	1.15	(1.03, 1.29)
Model 2			
Mastectomy	1.9251	6.86	(1.41, 33.44)
Radiation Therapy	1.8848	6.59	(1.35, 32.16)
Cardiopulmonary Comorbidity	0.1185	1.13	(1.01, 1.26)